

REMARKS

In the Office Action, claims 1 and 3-23 are rejected under 35 U.S.C. § 112, first paragraph; claims 1 and 3-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting; and claims 1 and 3-23 are rejected under 35 U.S.C. § 102 or § 103. Claims 1, 6, 9, 10, 18 and 20 have been amended, and claims 2-5, 13-15 and 23 have been canceled without prejudice or disclaimer. Applicants believe that the rejections have been overcome or are improper in view of the amendments and for the reasons set forth below.

In the Office Action, claims 1 and 3-23 are rejected under 35 U.S.C. § 112, first paragraph. In response, Applicants respectfully submit that a deposit of the microorganism, namely, *Lactobacillus paracasei* CNCM I-2116 has been made pursuant to PCT Rule 13 *bis* during the examination of the related International Application No. PCT/EP00/01797 and further pursuant to the Budapest Treaty. A copy of the documents relating to the deposit as discussed above was attached as Exhibit A to Applicants' Amendment previously submitted on December 30, 2003. Further, Applicants assert that the *Lactobacillus paracasei* CNCM I-2116 strain will be irrevocably and without restriction or condition released to the public upon issuance of a patent regarding this case. Therefore, Applicants believe that the requirements pursuant to the first paragraph of 35 U.S.C. § 112 have been satisfied.

Accordingly, Applicants believe that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

In the Office Action, claims 1 and 3-23 have been rejected under 35 U.S.C. § 102 or § 103 in view of EP 0861905. Applicants believe that the anticipation and obviousness rejections should be withdrawn as set forth below.

Of the pending claims at issue, claims 1, 6, 9, 10, 18, and 20 are the sole independent claims. Independent claim 1 recites a biologically pure culture of lactic acid bacterium belonging to a genus *Lactobacillus* capable of adhering to and colonizing an intestinal mucosa and capable of preventing infection of intestinal epithelial cells by rotaviruses wherein the lactic acid bacterium strain is capable of growing in presence of up to about 0.4% bile cells. Independent claim 6 recites a method for preparing an ingestible support material that uses the lactic acid bacterium strain. Independent claim 9 recites a method for the treatment of a disorder that administers to a patient suffering the disorder the lactic acid bacterium strain. Independent

claim 10 recites a pharmaceutical composition that includes the lactic acid bacterium strain. Independent claim 18 recites a method for preventing a disorder that includes administering the lactic acid bacterium strain. Independent claim 20 recites a food that includes the lactic acid bacterium strain. As amended, each of the independent claims now recite that the lactic acid bacterium strain is *Lactobacillus paracasei* CNCM I-2116.

The present invention relates to *Lactobacilli* strains that have the ability to prevent infection of the intestinal epithelial cells by rotaviruses, all of which events can cause diarrhea. The claimed strains are so-called probiotic strains. In this regard, they essentially survive the passage through the gut, and thus, arrive in the intestine in an essentially live form, such that the strains are still capable of successfully adhering to and colonizing in the mucosa. In addition, the claimed strains can interact directly with the rotavirus receptors by, for example, actively scavenging. This can be disadvantageous for the rotaviruses (see, Specification, p. 6, lines 14-17 and Example 2 on p. 12-14) where the claimed strain can provide an inhibitory activity/property against infestation of intestinal cells and rotaviruses. Applicants have also found that the claimed strain surprisingly exhibits anti-allergic properties in that the claimed strain has an impact on the synthesis of different immunological mediators, for example, decreasing IL-4 required for IgE secretion. See, Specification, p. 7, lines 20-28.

In contrast, Applicants believe that the cited art is distinguishable over the claimed invention. As previously discussed, each of the independent claims have been amended to further recite that the lactic acid bacterium strain is *Lactobacillus paracasei* CNCM I-2116 and thus essentially incorporates the feature of claims 5 or 15. Therefore, the anticipation rejection should be withdrawn in view of same.

Further, Applicants believe that the obviousness rejection is improper. EP0861905 relates to *Lactobacilli* strains useful in the treatment of various disorders of the gastrointestinal tract, such as peristaltic disorders, gastroenteritis, heartburn, flatulence and diarrhoea, particularly diarrhoea following the use of antibiotics (See, EP0861905, p. 6, lines 7-8) or after an anti-tumour radiotherapy (See, EP0861905, p. 5, line 10). Thus, the reference fails to provide whether the *Lactobacilli* are merely assisting in reconstituting the micro-flora of the intestine or whether they are also providing an activity against some particular agents.

For example, EP0861905 merely teaches that its strains are opposing “pathogens” presumably through a lowering of the pH of the intestinal environment. See, EP0861905, p. 4, lines 33 to 35. As the term “pathogen” is not specifically defined, this term can be understood to have a number of different meanings, such as parasites (like worms), fungi, bacteria, viruses or even particles like prions or of inorganic nature. Thus, Applicants believe that the teachings of EP0861905 are insufficient in scope and detail to cover viruses, let alone rotaviruses, in contrast to the claimed invention.

Further, EP0861905 fails to provide any information relating to a protection or inhibitory property against infection of intestinal epithelial cells by rotaviruses. Again, EP0861905 teaches that the lactobacilli oppose against pathogens through a lowering of the pH of the intestinal environment. See, EP0861905, p. 4, lines 31-35. Yet, it is not clear how this affects any of the “pathogens” that may be contemplated as embraced by this term as discussed above. Indeed, rotaviruses exhibit a relatively high stability and will presumably not be affected by a relatively small lowering of the pH of the extracellular and intestinal environment caused by organic acids. Thus, one skilled in the art would rather conclude that the strains of EP0861905 (which act by lowering the pH) are not capable of a prevention of an infection of the human intestine brought about by rotaviruses in contrast to the claimed invention.

The emphasis of EP0861905 relates to a process which allows the selection of Lactobacilli strains exceedingly viable and resistant to technological treatments, such as freeze-drying or mixing with excipients, which strains are useful for the therapeutical and prophylactic treatment of disorders of the gastrointestinal system in humans. See, EP0861905, p. 2, lines 46 to 48. Clearly, this fails to disclose or suggest that micro-organisms are actively participating in the treatment of diarrhoea brought about by rotaviruses and are, indeed, present in nature at all and thus can be isolated in contrast to the claimed invention. In fact, neither viruses as such, nor in particular rotaviruses causing diarrhoea are mentioned in EP0861905 as previously discussed.

In addition, EP0861905 fails to disclose or suggest that such a micro-organism having the protective properties as claimed can arrive in the intestine in an essentially live form, adhere to the intestine’s mucosa and colonize it. Once implanted in the mucosa (or even before), the claimed strain can exert its beneficial effects, for example, by directly interacting with cellular

rotavirus receptors as the claimed strains. This can be done by actively scavenging rotaviruses. Clearly, this is different as compared to lowering the pH as disclosed in EP0861905.

Additionally, in contrast to the claimed strains, EP0861905 prefers a mixture of strains. See, EP0861905, page 5, lines 36-43. In this regard, one skilled in the art would necessarily conclude that just one strain may not be sufficient for gaining successful treatment based on the teachings of EP0861905. Again, the claimed strain is a *Lactobacillus paracasei* CNCM I-2116 as previously discussed.

Of further importance, the claimed strains have an anti-allergenic property that has an impact on the synthesis of various immunologically active mediators. Generally, T-cell responses are differentiated into Th-1-type and Th-2-type responses, while the latter is responsible for the differentiation of humoral immune responses. Th-2 cells produce high amounts of IL-4 which is a cytokine responsible for the secretion of IgE and the major antibody class involved in allergic reactions. As demonstrated in the specification in Example 6, ST11 induces an up to 8-fold decrease in IL-4 production. On the other hand, ST11 strongly enhances IL-12 production of adherent cells, which is a cytokine required for the induction of Th-responses. Accordingly, it is believed that the claimed strains additionally display properties that can modulate the immune response by reducing and/or preventing ongoing allergic reactions. Therefore, Applicants believe that the claimed strains and method of use thereof as further claimed are distinguishable from EP0861905.

Based on at least these reasons, Applicants believe that the cited reference is deficient with respect to the claimed invention. Therefore, Applicants believe that the cited reference fails to disclose or suggest the claimed invention.

Accordingly, Applicants respectfully request that the anticipation and obviousness rejections in view of EP0861905 be withdrawn.

In the Office Action, claims 1 and 3-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting. More specifically, claims 1 and 3-23 are provisionally rejected as allegedly being unpatentable over claims 1-22 of copending application No. 09/936,489 and claims 1-2 and 4-22 of copending application No. 09/936,452. As the obviousness-type double patenting rejections are provisional, Applicants assert that they plan to submit a terminal disclaimer, if necessary, to overcome the provisional rejections once either one

or both of the copending applications have issued. Therefore, Applicants believe that they have been responsive to the provisional rejections at this stage in the prosecution.

For the foregoing reasons, Applicants respectfully submit that the present application is in condition for allowance and earnestly solicit reconsideration for the same.

Respectfully submitted,

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